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EXAMINER	
COUNTS, GARY W	
ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/921,004	Applicant(s) ANDERSON ET AL.	
	Examin r Gary W. Counts	Art Unit 1641	

-- Th MAILING DATE of this communication app ars on th cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *03 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Oath/Declaration

> It does not identify the mailing or post office address of each inventor. A mailing or post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing or post office address should include the ZIP Code designation. The mailing or post office address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

Drawings

The drawings are objected to because Figures 1A-AD should be amended to include all vertical and horizontal units. Further, Figure 3 requires molecular weight units.

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because the section entitled Brief Description of the Drawings needs to describe each figure of figure 1 (i.e. 1A-1D). Correction is required. See MPEP § 608.01(b).

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claim 13 recites the affinity column comprises recombinant microorganism display antibodies. On page 6, lines 10-17 of the specification, Applicant provides a list of immunologic and non-immunological affinity materials. However, recombinant microorganism display antibodies are not disclosed in the specification.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claims 10 and 11 recites reverse phase stationary phase is a non-porous C18 material. On page 6, lines 4-6 of the specification, Applicant discloses that conditions such as, but not limited to, for example, pH, mesh size, flow rates and stationary phase media selection can be modified to select for specific low molecular weight patterns. However, reverse phase stationary phase is a non-porous C18 material is not disclosed anywhere in the specification.

Claim Objections

Claim 1 is objected to because of the following informalities: Claim 1, line 3 the recitation "separating fraction" should be --separating fractions--.

Claim 14 depends from claim 14. Claim 14 should depend from claim 13.

Claim 16 depends from claim 16. Claim 16 should depend from claim 15.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 the recitation "above about" is vague and indefinite. It is unclear what applicant intends. There is no definition provided for the term in the specification.

Claim 1 the recitation "the filtration limits of a normal kidney" there is insufficient antecedent basis for this limitation.

Claim 2, line 9 the recitation "the results of said detection" there is insufficient antecedent basis for this limitation.

Claim 2, line 11 "can be" is vague and indefinite. Is the biological sample correlated with physiological state or not?

Claim 2, line 12 "physiological state" is vague and indefinite. It is unclear what applicant is trying to encompass. The physiological state of what? (i.e. metabolism, toxicology, disease processes etc..). There is no definition or guidance provided for the term in the specification. See also deficiency found in claim 20.

Claim 5, line 20 "said concentrating step" there is insufficient antecedent basis for this limitation. See deficiencies throughout the claims.

Claim 10, line 1 "the elution" there is insufficient antecedent basis for this limitation.

Claim 15 "said affinity chromatography" there is insufficient antecedent basis for this limitation.

Claim 15 is vague and indefinite because it is unclear how the affinity column comprises monoclonal or polyclonal antibodies but it is considered to be a non-immunologic entity.

Claim 17, "said separating step" is vague and indefinite. It is unclear if this is the same step as the separating fraction having a molecular weight above about 3kDa and below the filtration limits of a normal kidney or if it is a separate step?

Claim 19, line 1 "said deflecting step" there is insufficient antecedent basis for this limitation.

Claim 20, the recitation "step (c)" is vague and indefinite. There is no step (c) recited in claim 1. It is unclear what portion of claim 1 applicant is referring to.

Claim 20 is vague and indefinite because data is not always fixed and the image can be changed. The generated data depends from different factors and therefore, the image is not consistent.

Claim 20 is vague and indefinite because it is unclear how an image provides linkage to an annotation.

Claim 21, line 15 "is adapted to" is vague and indefinite. It is unclear how the image displaying means is adapted.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, and 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al (US Patent 5,492,834).

Liu et al disclose a method for detecting proteins in urine and serum samples. Liu et al disclose applying the sample to a size exclusion gel. Liu et al disclose that the size exclusion gels have a molecular weight exclusion of at least 6,000. Liu et al disclose that these size exclusion gels fractionate proteins. Liu et al disclose recovering the fraction and separating and determining at least one analyte having an analyte molecular weight range greater than the exclusion molecular weight of the gel (col 8, lines 1-67).

5. Claims 1, 3, 4, 8, 9 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Myrick et al (Quantitative two-dimensional electrophoretic detection of possible urinary protein biomarkers of occupational exposure to cadmium, Applied and Theoretical Electrophoresis (1993), 3, 137-146).

Myrick et al disclose a method for determining a protein in a urine sample. Myrick et al disclose centrifuging (concentrating) the urine sample to remove particulate

matter. Myrick et al disclose removing analytes, polypeptides by subjecting the sample to centrifugal microconcentrator with a 10,000 Da cutoff membrane (fractionating). Myrick et al disclose recovering the retentate and performing two-dimensional electrophoresis

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-5, 8-11, 17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spahr et al (Towards defining the urinary proteome using liquid chromatography-tandem mass spectrometry, Proteomics Jan, 2001, 1 93-97) in view of Liu et al (US Patent 5,492,834).

Spahr et al disclose a method to detect proteins in a urine sample. Spahr et al disclose centrifuging the urine sample (page 94, col 2). Spahr et al disclose the urine sample can be fractionated by using affinity methods (page 96). Spahr et al disclose that these affinity methods can be used to remove albumin and other abundant components. Spahr et al disclose subjecting the sample to two-dimensional gel electrophoresis. Spahr et al disclose that the gel was visualized by silver staining and software and the protein spots were by in-gel digestion and subsequent liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis (page 94, col 2).

Spahr et al disclose that the Image of silver-stained 2-DE was enhanced by using Microsoft Photo Editor.

Spahr et al differ from the instant invention in failing to teach the concentrating step comprising separation of low molecular weight constituents by size exclusion chromatography.

Liu et al disclose applying a urine sample to a size exclusion gel. Liu et al disclose that the size exclusion gels have a molecular weight exclusion of at least 6,000. The use of such an exclusion gel provides methods for analyzing body fluid samples for certain analytes while eliminating the effects of the presence of interfering components and provides for methods for analyzing patient urine samples for low concentrations of proteins indicative of certain disease states.

It would have been obvious to one of ordinary skill in the art to incorporate size exclusion gels as taught by Liu et al into the method of Spahr et al because Liu et al shows that the use of such an exclusion gel provides methods for analyzing body fluid samples for certain analytes while eliminating the effects of the presence of interfering components and provides for methods for analyzing patient urine samples for low concentrations of proteins indicative of certain disease states.

8. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Spahr et al in view of Liu et al as applied to claims 1-5, 8-11, 17 and 19 above and further in view of O'Donnell et al (US 5,998,216).

See above for teachings of Spahr et al and Liu et al.

Spahr et al and Liu et al differ from the instant invention in failing to teach the addition of at least one protease inhibitor to the body fluid upon collection.

O'Donnell et al disclose the addition of protease inhibitor to urine. O'Donnell et al disclose that the addition of protease inhibitors to urine provides for maintaining and preserving the integrity of proteins and polypeptides present in a body fluid sample obtained ex-vivo (abstract). O'Donnell et al also disclose that these protease inhibitors provide a powerful effect on cytokines individually and collectively in human urine samples; and enhances markedly the stability and the preservation effect for the cytokines under a variety of different collection and environmental conditions (col 13, lines 1-56).

It would have been obvious to one of ordinary skill in the art to incorporate the use of a protease inhibitor such as taught by O'Donnell et al into the method of Spahr et al because O'Donnell et al shows the addition of protease inhibitors to urine provides for maintaining and preserving the integrity of proteins and polypeptides present in a body fluid sample obtained ex-vivo. O'Donnell et al also disclose that these protease inhibitors provide a powerful effect on cytokines individually and collectively in human urine samples; and enhances markedly the stability and the preservation effect for the cytokines under a variety of different collection and environmental conditions.

Claims 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spahr et al in view of Liu et al as applied to claims 1-5, 8-11, 17 and 19 above and further in view of Suzuki et al (US 5,246,835).

See above for teachings of Spahr et al and Liu et al.

Spahr et al and Liu et al differ from the instant invention in failing to teach an affinity column.

Suzuki et al disclose an affinity column couple with a monoclonal or polyclonal antibody specific for albumin (col 10, lines 10-15). Suzuki et al disclose that this affinity chromatography is advantageously used for the separation of human albumin and the fragments thereof (col 9, lines 39-43).

It would have been obvious to one of ordinary skill in the art to incorporate an affinity column such as taught by Suzuki et al into the method of Spahr et al and Liu et al because Spahr et al is generic for the affinity method used for the removal of albumin and further because Suzuki et al shows that this affinity chromatography is advantageously used for the separation of human albumin and the fragments thereof.

9. Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spahr et al in view of Liu et al and Suzuki et al as applied to claims 1-5, 8-14, 17 and 19 above, and further in view of Degen et al (US Patent 4,693,985).

See above for teachings of Spahr et al, Liu et al and Suzuki et al.

Spahr et al, Liu et al and Suzuki et al differ from the instant invention in failing to disclose the affinity chromatography is a non-immunologic entity.

Degen et al disclose Protein A used as an acceptor molecule in affinity chromatography, which provides for the removal of mammalian proteins from body fluids (col 12, lines 32-44).

It would have been obvious to one of ordinary skill in the art to incorporate protein A as taught by Degen et al into the modified method of Spahr et al because Degen et al shows that protein A provides for the removal of mammalian proteins from body fluids.

10. Claims 6 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spahr et al in view of Liu et al as applied to claim1-5, 8-11, 17 and 19 above, and further in view of Furst et al (US 5,926,387).

See above for teachings of Spahr et al and Liu et al.

Spahr et al and Liu et al differ from the instant invention in failing to teach zonal sedimentation centrifugation on density gradients.

Furst et al disclose a technique, which, involves layering a sample containing the components of interest onto the top of a liquid column, which is stabilized by a density-gradient of an inert solute. Furst et al disclose that this process is known as Rate-zonal sedimentation. Rate-zonal sedimentation is used to improve the efficiency of the fractionation by separating the particles according to size (col 1, lines 45-67).

It would have been obvious to one of ordinary skill in the art to incorporate rate-zonal sedimentation as taught by Furst et al into the modified method of Spahr et al because Furst et al shows that rate-zonal sedimentation improves the efficiency of the fraction by separating the particles according to size.

With respect to the stationary phases comprising different mesh sizes as recited in the instant claims, the mesh sizes can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no

more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

11. Claims 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spahr et al in view of Liu et al as applied to claims 1-5, 8-11, 17 and 19 above and further in view of Taylor, Jr. et al (US 6,301,377).

See above for teachings of Spahr et al and Liu et al.

Spahr et al and Liu et al differ from the instant invention in failing to teach an image comprising a pattern of data generated wherein the image provides linkage to an annotation.

Taylor, Jr. et al disclose an image processing method for warping a plurality of gel electrophoresis images. Taylor, Jr. et al disclose assigning tiepoints in a reference image and in one or more object images. The tiepoints in the object image are evaluated one-by-one by comparison to regions about a corresponding tiepoint in the reference image, and the location of the tiepoint in the object image is adjusted by slight movement to a location with respect to recognizable features in both the reference and

object image (abstract, and col 5, lines 20-67). Taylor, Jr. et al disclose that this method provides to bring multiple images of a single gel into registration with one another and provides meaningful comparisons between the multiple scans and/or a master pattern (col 7, lines 1-13).

It would have been obvious to one of ordinary skill in the art to incorporate gel electrophoresis images as taught by Taylor, Jr. et al into the method of Spahr et al because Taylor, Jr. et al shows that these images provides for meaningful comparisons between the multiple scans and/or a master pattern.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary W. Counts
Examiner
Art Unit 1641
October 28, 2002

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